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TOPICAL APPLICATION AGENT

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TOPICAL APPLICATION AGENT

[Gaiyozai]

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[There are no amendments to this patent.]

Claims

1. A topical application agent characterized by containing allantoin as an active component, caroxyvinyl polymer and water, and having its pH set below 5.5.

2. The topical application agent of Claim 1 containing no surfactant.

Detailed explanation of the invention

This invention pertains to a topical application agent containing allantoin as an active component. The topical application agent in this case means a medicinal or cosmetic formulation for topical applications to the face, hands, feet, etc., for maintaining them in a healthy state.

Allantoin is a compound described in standard cosmetic raw materials, used for treatment [illegible]s, burns, etc., and skin ailments such as eczema, etc., and in general, 0.1%-0.5% is [illegible]scribed. It has been known that allantoin is liable to be hydrolyzed, for example to glyoxylic [illegible]id and urea under acidic condition and allantoic acid under alkaline conditions, but no accurate [illegible]quantitative determination has been carried out, and thus, the reduction in its content with time is considered to be remarkable.

Therefore, the inventors of this invention studied diligently on a topical application agent with allantoin compounded to develop a product having a reduced allantoin content within an allowable range, causing no foul odor, discoloration, viscosity changes, etc., for a long period of time, and demonstrating excellent usability; and as a result, they arrived at this invention.

Specifically, this invention is a topical application agent containing allantoin as an active component, carboxylvinyl polymer and water, with its pH adjusted below 5.5.

The carboxyvinyl polymer of this invention is also found in standard cosmetic raw materials, it can be prepared by using acrylic acid as a main component and carrying out copolymerization with acrylate, etc., it has been known to exhibit excellent thickening effects upon neutralization, and it is commercially available with a trade name such as Carbopole, Jonlon, Highviswako, etc.

The amount of carboxyvinyl polymer to be compounded is generally in the range of about 0.1-1.0%, and it is said to exhibit the most excellent effects when neutralization to pH 5.5-11 is carried out by using an alkaline inorganic substance such as sodium hydroxide, potassium hydroxide, etc., or alkaline organic substance such as ethanolamine, etc. However, according to the results of a study carried out by the inventors of this invention on its use in a topical application agent of allantoin, the allantoin content was found to be reduced below 90% after long-term storage in some cases particularly, when the pH was 5.5 or higher on the alkaline side. Therefore, the possibility of using the compound at pH below 5.5 was evaluated. As a result, it was possible to prepare a topical gel application formulation in a colloidal, chemically stable state, and also a bacteriocidal effect of low pH was observed.

The topical application agent of this invention may be compounded with components other than allantoin, carboxyvinyl polymer and water, as conventionally compounded in topical application agent formulations. For example, as oily components showing skin-protecting action, there are hydrocarbons such as vaseline, fluid paraffin, squalane, etc., higher alcohols such as cetyl alcohol, stearyl alcohol, etc., and higher fatty acids such as palmitic acid, stearic acid, etc. Furthermore, as moisture-retaining agents, there are glycerol, sorbitol, propylene glycol, etc., as preservatives, there are phenol derivatives such as methyl hydroxybenzoate, etc., benzalconium chloride, sorbic acid, dehydroacetic acid, boric acid, etc., and furthermore, perfumes and coloring agents may be also used. In addition, for formulating ointments, creams, etc., a surfactant,

especially a synthetic surfactant, is frequently used as an emulsifier. There are, for example, nonionic surfactants such as sorbitan fatty acid ester (Span), polyoxyethylene sorbitan fatty acid ester (Tween), polyoxyethylene glycol alkyl ether, polyoxyethylene glycol fatty acid ester, etc., cationic surfactants such as benzalconium chloride, benzetonium chloride, etc., and anionic surfactants such as sodium alkylsulfate, etc. It is possible to prepare a colloidal, chemically stable cream by using a surfactant, but the use of a surfactant is not preferable with respect to skin irritation and skin toxicity.

In the topical application agent of this invention, the use of surfactants is possible but not essential, and it is characterized by having excellent usability and stability with time, even if no surfactant is compounded.

Any of those conventional processes for the production of topical application agent formulations may be used. For example, oily components such as paraffin, squalane, etc., and aqueous components such as glycerol, propylene glycol, water, etc., are respectively heated at 50-80°C, and subsequently, are mixed while stirring. Subsequently, the mixture is cooled to room temperature while stirring. The carboxyvinyl polymer may be added to the oily components or, after dispersing in the aqueous components, it is dissolved uniformly.

This invention is explained in detail by using application and comparative examples as follows.

Application example

Allantoin	0.4 parts by weight
Carbopole 934	1.0 part by weight
Squalane	10.0 parts by weight
1,3-Butyelne glycol	5.0 parts by weight
Ethyl paraoxybenzoate	0.1 part by weight
Sodium hydroxide	Suitable amount
Purified water	Make up the total amount to 100 parts by weight

Carbopole 934 (Goodrich carboxyvinyl polymer) was uniformly dispersed in squalane to obtain an oily component suspension. On the other hand, purified water was heated to about 50°C, ethyl paraoxybenzoate, 1,3-butylene glycol and allantoin were added while stirring, dissolved, subsequently the oily component prepared as described above was added, and the mixture was stirred for 10 min. Subsequently, sodium hydroxide was added to adjust to pH 4±0.2, 5±0.2, 6±0.2 or 7±0.2, and the mixture was cooled to room temperature while stirring.

Comparative Example 1

o/w emulsion hydrophilic ointment (10th revised edition of Pharmacopoeia Japonica)

Allantoin	0.4 parts by weight
White Vaseline	25.0 parts by weight
Stearyl alcohol	22.0 parts by weight
Propylene glycol	12.0 parts by weight
Sodium laurylsulfate	1.5 parts by weight
Ethyl paraoxybenzoate	0.025 part by weight
Propyl paraoxybenzoate	0.015 part by weight
Purified water	Make up the total amount to 100 parts by weight

White Vaseline and stearyl alcohol were dissolved over a water bath, the solution was maintained at about 75°C while stirring, allantoin dissolved in purified water and heated at 75°C was added, and the mixture was stirred until solidified.

Comparative Example 2

w/o emulsion water-absorbed ointment (10th revised edition of Pharmacopoeia Japonica)

Allantoin	0.4 part by weight
White Vaseline	40 parts by weight
Cetanol	18 parts by weight
Sorbitan sesquioleate	5 parts by weight
Lauromacrogols	0.5 part by weight
Ethyl paraoxybenzoate	0.1 part by weight
Propyl paraoxybenzoate	0.1 part by weight
Purified water	Make up the total amount to 100 parts by weight

White vaseline, cetanol, propyl paraoxybenzoate, lauromacrogols, and sorbitan sesquioleate were heated to 75°C over a water bath and dissolved to obtain an oily component mixture. Separately, allantoin and ethyl paraoxybenzoate were added to purified water and heated to 80°C to obtain a solution which was gradually added to the oily component mixture while stirring, heating was stopped, and the mixture was stirred until solidified.

Comparative Examples 1 and 2 were hydrophilic ointment and water-absorbed ointment of the 10th revised edition of Pharmacopoeia Japonica with allantoin compounded.

The application example and comparative examples prepared as described above were used by 5 panel members to carry out an organoleptic test with respect to stickiness, spreadability and refreshing feeling at the time of usage.

The results obtained are shown in Table 1. The topical application agent of the application example was found to be most excellent with respect to stickiness, spreadability and refreshing feeling at the time of usage.

Table 1

Sample	Stickiness	Spreadability	Refreshing feeling after application
Caroboxyvinyl polymer-added topical application agent	No stickiness	Good	Refreshing
o/w (hydrophilic ointment)	Slight stickiness	Good	Slightly poor refreshing feeling
w/o emulsion (water-absorbed ointment)	Sticky	Slightly poor	Poor refreshing feeling

The topical application agent of the application example was stored at room temperature for 8 months or 40°C for 3 months, and subsequently, the appearance (naked-eye observation), usage feeling and allantoin content were determined to obtain the results shown in Table 2.

Table 2

①測定項目	②試料 / ③保存条件	④実施例の外用剤 pH 4	pH 5	pH 6	pH 7
⑤外観（肉眼判定）	室温8ヶ月	変化なし	変化なし	変化なし	変化なし
	⑧ 40°C 3ヶ月	⑨〃	〃	〃	〃
⑥使用感（官能評価）	室温8ヶ月	〃	〃	〃	〃
	⑧ 40°C 3ヶ月	〃	〃	〃	〃
⑦アラントイン含量（開始時を100%）	室温8ヶ月	100%	100%	98%	98%
	⑧ 40°C 3ヶ月	97%	96%	76%	37%

Key:
1 Item measured
2 Storage condition
3 Sample
4 Topical application agent of the application example
5 Appearance (naked-eye observation)
6 Usage feeling (organoleptic test)
7 Allantoin content (before storage: 100%)
8 Room temperature for 8 months
40°C for 3 months
9 No change

The allantoin content was determined quantitatively by using high performance liquid chromatography..

As apparent from the results shown in Table 2, those samples of the topical application agent of this invention prepared with their pH in the range of 4-7 showed no changes in appearance and usage feeling after storage at room temperature for 8 months or 40°C for 3 months. However, the results with respect to allantoin content showed that those samples prepared at pH 4 and pH 5 were excellent, and the allantoin content was found to be reduced at pH 6-7.

Incidentally, if the topical application agent of this invention is adjusted below pH 4, it is not desirable for the skin, and it is suitable to adjustment into the range of pH 4-pH 5.5.